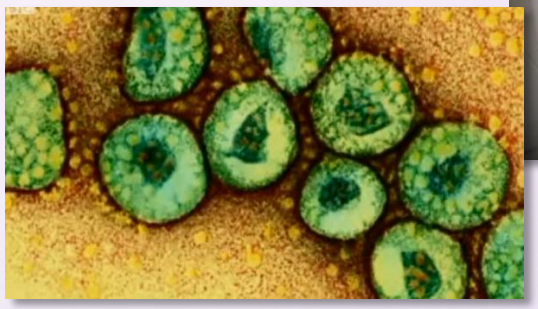

EMERGING INFECTIONS: THE PLAIN OL' CLINICAL LABORATORY PERSPECTIVE

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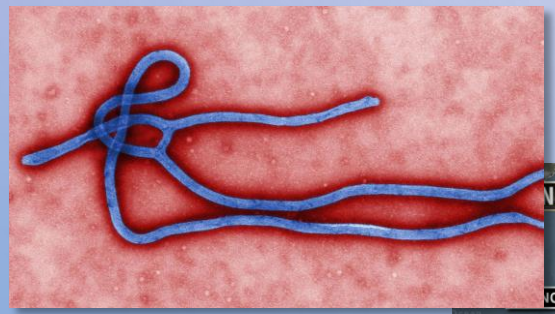
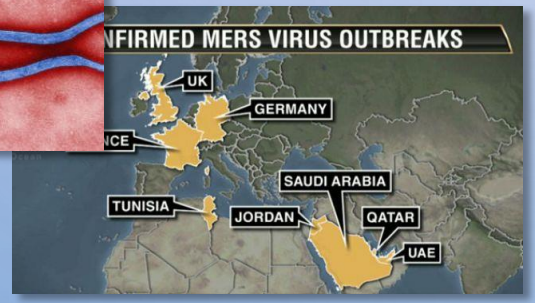




OBJECTIVES

- Laboratory Response to Emerging Infections
  - In the ***Emerging Phase***
    - How to do a risk-assessment.
    - Risks associated with routine clinical laboratory instrumentation and processes.
    - Balancing risks to laboratory staff and patients.
    - How do we deal with / address duty to provide care in the laboratory environment.
  - How do we monitor and improve safety in the ***routine*** laboratory environment?

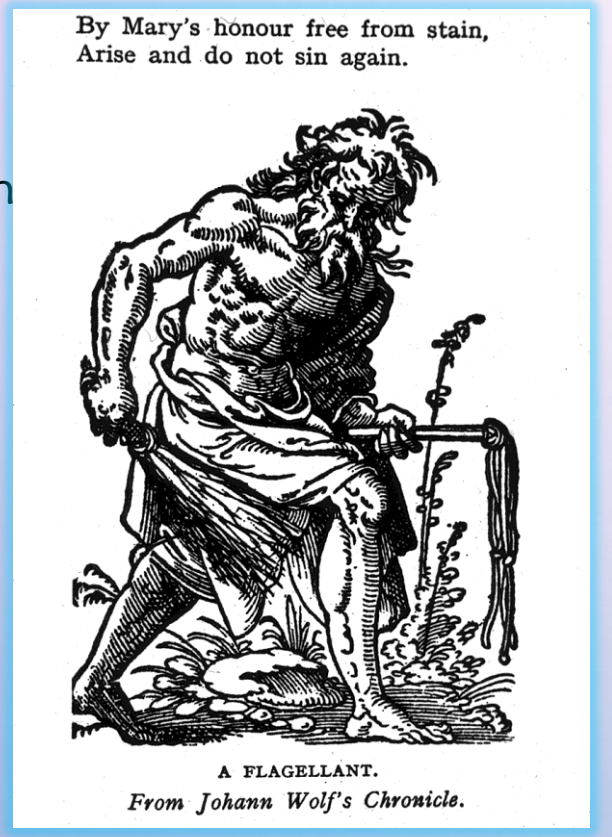
EMERGING INFECTIONS IN CONTEXT

PLAGUES HAVE BEEN A PART OF HUMAN EXISTENCE DURING RECORDED HISTORY; AND HAVE HAD A DEEP IMPACT ON SOCIETIES.

FOUR HORSEMEN OF APOCALYPSE, BY VIKTOR VASNETSOV. PAINTED IN 1887. FROM LEFT TO RIGHT, THEY ARE DEATH/PLAGUE ON THE PALE HORSE, FAMINE ON THE BLACK, WAR ON THE RED, AND A RIDER WHOSE IDENTITY IS UNCLEAR IN THE REVELATION TEXT ON THE WHITE.

REACTIONS TO INFECTIOUS DISEASES

Self-punishm



A FLAGELLANT.
From Johann Wolf's Chronicle.

'Best Pra

Persecut

BURNING OF PLAGUE SPREADERS.
From Sebastian Muenster's "Cosmographie."

RISK ASSESSMENT FOR LABORATORY INFECTION

- Route of Transmission – How do I get it?
  - Blood-borne
  - Contact
  - Droplets
  - Aerosol
- Samples at risk – Where is the virus?
  - Respiratory only vs. blood, urine, etc.
- Prevalence – How much of it is there?
  - Common vs. rare
- What procedures within the laboratory generate risk?

RISK ASSESSMENT NEEDS

- To do risk assessments well, clinical laboratories need:
  - Reliable information on the biology of the threat
  - Reliable and up-to-date information on the epidemiology of the threat
  - Detailed information on laboratory operations and equipment in the context of the above information.
    - For most laboratories, a template would be extremely helpful.
    - We don't have time to re-invent the wheel, and some of us aren't that good as wheel-inventors.
    - Information on instrument-related risks seems hard to come by.

INSTRUMENTATION AND PROCESSES

PRE-ANALYTIC

SAMPLE COLLECTION

TRANSPORT

RECEPTION AND UNPACKING

CENTRIFUGATION

UNCAPPING

ALIQUOTING

TRANSPORT WITHIN THE LAB

TRANSPORT TO REFERENCE LABS

ANALYTIC

CHEMISTRIES

BLOOD GASES

HEMATOLOGY

BACTERIOLOGY

VIROLOGY

MOLECULAR TESTING

TRANSFUSION MEDICINE

POST-ANALYTIC

WASTE MANAGEMENT

SAMPLE STORAGE - RETRIEVAL

RISKS IN THE ANALYTIC PHASE 1

- Chemistry
  - Complex analyzers with multiple sampling stations, aliquoting events, and waste pathways.
    - Many cannot perform closed-tube sampling
    - Require frequent periodic maintenance, service.
    - Extremely expensive; critical for care of large numbers of patients.
- Blood Gases
  - Sample submitted in syringe
  - Extremely labile sample requires rapid handling
- Hematology
  - Complex analyzers as above
  - Manual or automated slide-making; glass slides.

RISKS IN THE ANALYTIC PHASE 2

- Bacteriology
  - Survival of emerging viruses in culture media generally unknown, but likely (old studies show HIV does)
  - Much manual handling of samples and cultures
  - Complex analyzers as above
- Virology
  - Growth of emerging pathogens in viral culture (waning in importance as labs abandon viral culture)
- Molecular diagnostics
  - Complex analyzers as above.
  - Many manual or semi-manual methods in some laboratories.
  - How to validate EUA tests for dangerous, rare pathogens?

RISKS IN THE ANALYTIC PHASE 3

- Transfusion Medicine
  - Tube-based methods likely generate droplets
  - No sealed-rotor blood bank centrifuge is currently available, per my local colleague.
  - Risks associated with gel or instrumented methods unknown.

BALANCING RISKS

- A thorough risk-assessment should allow laboratories to minimize risks
  - Many unknowns
    - Biology of emerging agent
    - Interaction of that biology with complex instrumentation and systems
  - Certainty, in an emerging infection, is unlikely
  - Risk to laboratory workers will remain
- Laboratories exist to provide patient care
  - Limiting test menus may (probably will) compromise care for some patients
  - Contaminating a laboratory, or infecting laboratory workers, may compromise care for large numbers of patients.

WHAT EMORY AND NEBRASKA DID

Aspect of Testing	Emory University Hospital	Nebraska Medical Center (NMC)
Location(s) performing testing	Self-contained laboratory within the quarantine facility only.	POC tests within the biocontainment unit (BCU) Open-tube tests in BSL-3 suite of Nebraska Public Health Laboratory (NPHL); Closed-tube tests in NMC core lab
Menu of tests made available within treatment area	Chemistry profiles (Chem7; Mg, PO4, liver profile) Arterial blood gases PT/INR Rapid malaria antigen BioFire Biothreat molecular panel	Centrifugation of samples Chem 8 profile PT/PTT ABO/Rh slide agglutination malaria smear preparation Urine dipstick rapid HIV; rapid RPR
Menu of tests performed elsewhere	none	*NPHL:* EUA Ebola PCR and BioFire Biothreat molecular panel Blood cultures with stationary incubation and daily blind subculturing Specimen repository and shipping *NMC Core Lab:* Broad range of blood and urine chemistries CBC Malaria smear interpretation

WHY EMORY AND NEBRASKA DON'T HELP MUCH

- These facilities have a high probability of seeing patients with EBV disease
  - Most of the rest of us have a lower probability
  - Can we justify the same allocation of resources?
- These facilities are planning primarily for patients with diagnosed EBV disease
  - Managing a patient with diagnosed EBV disease requires primarily critical-care tests; blood gases, electrolytes, blood counts.
- The rest of us have to plan for patients for whom EBV disease is on a long list of possibilities
  - Requires diagnostic testing for essentially every travel-associated and non-travel-associated fever + fatigue syndrome.
  - Can these tests wait until the patient rules-out?

STAFFING THE LAB

- Can we rely on volunteers?
  - Many fewer laboratory staff within each specialty than nursing/physician staff
  - Small numbers = less redundancy
- Where does duty of care reside?
  - Employment contracts?
  - ASCLS Code of Ethics
    - Non-binding; unspecific

WHERE ARE WE?

- Anecdotally, few laboratories are limiting their precautions to CDC recommendations.
  - Per ClinMicroNet since last September
- Most are limiting core-lab testing severely on rule-out patients.
  - Limited menu of high-impact tests (e.g. electrolytes, malaria testing) prior to rule-out
  - Use of Point of Care devices to limit transport / exposures
    - No data on the safety of this practice

ISSUES (ALMOST) EVERYONE CAN AGREE ON; MINIMALLY, ON EBOLA

- A well-defined system to identify suspect patients and address appropriate labeling of specimens and notification of lab personnel *before* the specimen is sent.
- Limit testing to essentials for acute care.
- Track personnel who handle and work with samples from suspect patients.
- PPE must be available in the lab and used rigorously. Are sufficient supplies available?
- Specimen transport issues: no pneumatic tubes, containment of primary specimens. Rigid specimen containers that can contain spills if they occur.
- Centrifugation in closed protective systems, inspect for leakage before opening.
- Removal/disposal strategy for PPE. Laboratory to drill don/doff procedures per CDC training materials.
- Procedure for cleaning/disinfecting chemistry/hematology equipment (if used) per manufacturer's guidelines. Find and assess.
- Address Microbiology and other manual processes.
- Blood bank: Consider electronic crossmatch and O- blood for patients without risk factors for alloantibodies to minimize manual procedures. See AABB guidelines at http://www.aabb.org/press/Pages/Infection-Control-for-Handling-Blood-Specimens-from-Suspected-Ebola-Patients.aspx.
- A simple plan that's well-implemented by trained staff is better than a complex plan that's badly implemented. Practice your plan.
- Protect the patients.

GAPS 1

- How much potential is there for transmission of emerging infections (name your favorite) via local short-range droplets or aerosols generated by laboratory instruments or procedures and affecting personnel in proximity to the event?
  - What is the likelihood of generation of small droplets / aerosols by typical clinical laboratory equipment?
  - What can we reasonably expect to get from vendors/CDC/FDA on this subject?
  - Is 'routine cleaning' enough? How do we know?
  - Will instruments which have been used for r/o patients who rule-in be serviced by vendors, or will we have to throw away a half-million dollar analyzer? Because that would be bad.
- How do we, for rule-out patients of arbitrary levels of risk (as opposed to those with established diagnoses of horrible disease X), balance the need to provide standard of care for those patients with the downsides of handling those samples in our laboratories, including:
  - risk to lab staff
  - interference with normal laboratory workflow and possibly harming other patients
  - risk of contaminating / bringing down essential instrumentation and REALLY harming other patients
  - other things I haven't thought of yet

GAPS 2

- There are contradictions between:
  - different guidelines (CDC vs ASM vs…)
  - different elements of the same guidelines, esp. "Some laboratory testing may need to be conducted and should not be delayed during patient evaluation and prior to definitive patient status" versus the uncertain status of many instruments.
- What to do about Blood Bank testing?
  - It's disingenuous to claim that 'rule out' patients shouldn't need transfusion.
  - Are automated or semi-automated methods safe enough to use in these patients?
- Personnel morale and requirement to work on risky specimens. How does professional duty to provide care apply to and translate into the laboratory environment and apply to workers at various levels?

REACTIONS TO INFECTIOUS DISEASES

…AND OCCASIONAL HEROISM

FROM CARLO COPPOLA'S PAINTING OF NAPLES'S PIAZZA MERCATO AS IT APPEARS IN 1657 DURING AN EPIDEMIC THAT KILLS 150 THOUSAND PEOPLE, HALF THE POPULATION OF NAPLES.

Two 17th Century Italian Plague Paintings

A priest gives communion to plague victims while at the same time keeping his distance and covering his face. He is in a difficult position. Many priests die in epidemics, but the Church considers plague punishment for sin. An honorable priest should have little to fear. So, is this priest a coward for taking precautions? No, no one working in this piazza could be considered a coward. Braver still is his assistant. Do you see him, passing out communion wafers? He does not even have a kerchief over his face.

ACKNOWLEDGEMENTS

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